

In the Specification:

Please amend the Title as follows:

GENE-CLUSTER-DNA ENCODING A POLYPEPTIDE REQUIRED FOR  
BIOSYNTHESIS OF TA ANTIBIOTIC

Amend the Abstract as follows:

There is provided ~~a purified, isolated and cloned~~ DNA sequences isolated from *Myxococcus xanthus* partially encoding a functional portion of a polypeptide component required for the synthesis of antibiotic TA. Also provided are purified, isolated and cloned DNA sequences encoding a polypeptide component required for postmodification of antibiotic TA and encoding a gene product involved in the regulation of the biosynthesis of antibiotic TA. A purified, isolated and cloned DNA sequence having a DNA sequence (seq. ID No: 21 and 202) encoding a polypeptide component required for encoding the TA gene cluster and any mutations thereof is provided. Also provided are methods of using the TA genes for combinatorial genetics and of using the TA genes encoding for synthesis and modification or regulation of antibiotic TA.

On page 1, line 3 (under Title), insert the following:

CROSS REFERENCES TO RELATED APPLICATIONS

This is a continuation-in-part of U.S. Patent Application No. 09/240,537, filed January 29, 1999, now abandoned.

Amend the paragraph beginning on page 3 line 11, as follows:

According to the present invention, there is provided a purified, isolated and cloned DNA sequence partially encoding a functional portion of a polypeptide component required for the synthesis of antibiotic TA. Also provided are purified, isolated and cloned DNA sequences encoding a polypeptide component required for postmodification of antibiotic TA and encoding encoding a gene product involved in the regulation of the biosynthesis of antibiotic TA. A purified, isolated and cloned DNA sequence having a DNA sequence (Seq. ID NO: 21 and 202) encoding a

polypeptide component required for encoding the TA gene cluster and any mutations thereof is provided. Also provided are methods of using the TA gene cluster and any mutations thereof is provided. Also provided are methods of using the TA genes for combinatorial genetics and of using the TA genes encoding for synthesis and modification or regulation of antibiotic TA.

Amend the paragraph beginning on page 4 line 12, as follows:

The present invention consists of ~~a-DNA sequences isolated from of at least 42 kb *Myxococcus xanthus* TA gene cluster of at least 42 kb, encoding peptides genes involved in TA production, and *Myxococcus xanthus* as best shown in Seq ID NOs:1 and 3-19~~through 17 and cosmid clones containing the entire TA gene DNA sequences. The TA gene cluster has been purified, isolated and cloned. The purification, isolation and cloning was done according to the methods described in Marshak et al, "Strategies for Protein Purification and Characterization. A laboratory course manual" CSHL Press, 1966.

Amend the paragraph beginning on page 4 line 20, as follows:

A DNA fragment of at least 42 kb (Figure 1), encoding genes involved in TA production in *Myxococcus xanthus* has been identified, cloned and analyzed. These steps were done in accordance with Marshak et al, "Strategies for Protein Purification and Characterization. A laboratory course manual" CSHL Press, 1966. This fragment consists a large region (designated Region 2) of about 20 kb, encoding the polypeptides TaA, TaB, TaC, TaD, TaE, TaF, TaG, TaH, TaI, TaJ, TaK, TaL, TaM, TaN, TaR3, TaR2 and TaR1, the genes which are responsible for the regulation of the post-modification of TA. An additional fragment (designated Region 1) of approximately 8-10 kb is located 10-20 kb downstream of the post modification region, encodes encoding the TaI the enzyme polypeptide. The TaI polypeptide is responsible for involved in the incorporation of the glycine into the TA polyketides chain. This novel polypeptide is made up of a peptide synthetase unit lying between two PKS modules.

On page 5, line 14, please insert the following two tables:

**Table 1**

Polypeptides encoded by the TA gene cluster of *Myxococcus xanthus*

<u>SEQ ID NO.</u>	<u>Function</u>
<u>1</u>	<u>Ta1 - synthetase unit and a PKS module</u>
<u>3</u>	<u>TaR1 – a surface layer protein</u>
<u>4</u>	<u>TaR2 – two component system, response regulator</u>
<u>5</u>	<u>TaR3 – two component system, kinase sensor</u>
<u>6</u>	<u>TaA – NUS-G like transcription antiterminator</u>
<u>7</u>	<u>TaB – an ACP</u>
<u>8</u>	<u>TaC – beta-ketoacyl (ACP) synthase III (KAS III FabH)</u>
<u>9</u>	<u>TaD – membrane associated protein</u>
<u>10</u>	<u>TaE – an ACP</u>
<u>11</u>	<u>TaF - beta-ketoacyl (ACP) synthase III (KAS III FabH)</u>
<u>12</u>	<u>TaG – signal peptidase II (LSPA)</u>
<u>13</u>	<u>TaH – cytochrome P450 hydroxylase (cP450)</u>
<u>14</u>	<u>TaI – malonyl CoA (ACPP transacylase (MCT, FabD)</u>
<u>15</u>	<u>TaJ – malonyl CoA (ACPP transacylase (MCT, FabD)</u>
<u>16</u>	<u>TaK – 3-oxoacyl (ACP) synthase (KAS I, FabB)</u>
<u>17</u>	<u>TaL – enoyl CoA hydratase</u>
<u>18</u>	<u>TaM – enoyl CoA hydratase</u>
<u>19</u>	<u>TaN – O-methyltransferase (fragment)</u>

PKS – polyketide synthase

ACP – acyl carrier protein

**Table 2**

DNA sequences identified from the TA gene cluster of *Myxococcus xanthus*

<u>SEQ ID NO.</u>	<u>Description</u>
<u>2</u>	<u>Nucleotides 1 - 7178</u>
<u>20</u>	<u>Nucleotides 1 - 19053</u>

On page 10 line 10 please amend the citation as follows:

3. Varon *et al.*, ~~1992.~~ Mutation and mapping of genes involved in production of the antibiotic TA in *micrococcus xanthus*. Antimicrob. Agents Chemother. 36: 2316-2321 (1992).